Referee report of the dissertation thesis "Noncovalent Interactions in the Gas Phase and Aqueous Solution: Theoretical Study" by Lucie Zendlová

The work is a piece of a focused effort on the subject of DNA basis and DNA base pairs, their solvation and interactions, in as well as out of the framework of DNA molecule. Last but not least one part of the thesis is dedicated to DNA intercalators design and properties, apparently one of the desirable aims of a theoretical description of the most important biomolecule in a cell. The series of 4 published papers (the author is the first author in 2 of them) and 2 manuscripts submitted or in preparation shows that applicant is able to succeed at the very competitive field of research in very good journals. On the other hand, I do not see too much of sense to add also a manuscript in preparation which did not meet requests of particular journal yet. This part, or its shortened version, would be much better to include into the thesis text.

The work has two faces and I am sorry to say that one of them is quite disappointing. The first face – the scientific one, is a pleasure to read and follow the ideas and data making connection between the ideas and conclusions. This first face is apparent a bit in the Summary of the thesis and fully in the articles attached. The second face – the way how the author deals with language issue is a pain. It is evident that the final version of the thesis never went for language correction and that some of the 51 pages long text part were made in a hurry. It makes the final judgment quite ambiguous. I assume that it would not be the same case if the thesis would be written in Czech language, but the level of English is not satisfactory regarding the level of the scientific part.

Apart of this issue there are few things which are worth to discuss in more details and one part of the thesis should be a discussion. I especially miss the opportunity to see all the results presented in the articles in a broader context and author's opinion regarding the complexity of the studied problems. I hope that author will present her conclusion and opinion during the thesis defense. I can't help but ask some questions I did not find answer in the presented thesis.

1) Do you think that the sampling of the FES in the case of base pairs solvation was comprehensive enough for comparison with the PES? Did you ever observe different results upon different initial conditions? Did you try other

force fields to make sure that the sampling is uniform and independent on the force field type?

2) It looks like that AT behaves differently than GC upon solvation. The question is if the different preferences for stacked and H-bonded pairs are not just a consequence of H bonds number between basis and therefore a number of waters available to replace them. What would be the situation for 3 water molecules interacting with GC pairs? This is exactly the question which must be connected with compensation of intermolecular H-bonds lost . Are you aware of any recent calculations focused on this fact?
3) The modification of nucleobasis is mentioned in connection with genetic engineering, nanotechnology and molecular electronics. What do you actually mean by the "extension of genetic alphabet via base analogues can lead to extension of amino acid groups and creation of artificial proteins or enzymes which can catalyze new reactions" Can you schematically show the principles of such processes and behaviour?

Regarding to the quality of the scientific aspect and its presentation in attached manuscripts I recommend the thesis for further proceeding.

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